National Institute of Allergy and Infectious Diseases
National Institutes of Health

June 29, 2005

UNITS FOR HIV/AIDS CLINICAL TRIALS NETWORKS

SUPPLEMENTAL QUESTIONS AND ANSWERS

Clinical Trials Units

1. In the event that no Network Leadership is funded for a given high-priority research area, what will happen to CTUs that propose research in that area?

DAIDS expects to fund applications in each of the six high-priority research areas described in the RFA. In the unlikely event that the structure resulting from this competition does not encompass all six priority research areas, it is expected that DAIDS will issue a subsequent competition to address research in those areas.

2. The network to which I hope to affiliate has asked that Clinical Research Sites maintain a capacity of an average of 40 participants on study per month, which is more than the average of 20 participants on study per month that is specified in the RFA. How does this impact my application and budget?

Applications will be evaluated by the Special Emphasis Panel against the core capacity requirements stated in the RFA, that is, an average of 20 participants on study per month over a 12 month period. The core budgets of applicants should also reflect the core capacity of 20. Applicants that wish to demonstrate capacity for a higher level of activity should include a description of their plans to increase enrollment and the requirements, including financial resources, in a separate section of the research plan and identify it accordingly. Since the financial resources necessary to support this increased activity will come from Network Protocol Implementation Funds, applicants should be careful not to include these financial requirements in the core budget proposed.

Clinical Research Sites

3. Can an institution that is submitting an application for a CTU with a Clinical Research Site at the same location also have that Clinical Site included in the application of another CTU?

Yes. A Clinical Research Site can be included in up to 2 CTU applications.

4. Is there a limit on the frequency with which satellite sites can be utilized?

There is no established limit on the frequency with which a satellite clinic can be utilized. However, if a satellite clinic is expected to be used very frequently, applicants are encouraged to examine whether that particular site could be organized as a fully functioning Clinical Research Site. Please see the amendment to the Units for Clinical Trials Units RFA regarding satellite sites posted at http://grants.nih.gov/grants/guide/notice-files/NOT-AI-05-038.html .

5. What is the process by which DAIDS will eliminate and/or replace non-productive Clinical Research Sites?

After the awards are made, DAIDS will work with Network Leadership and the Managing Partners to determine a fair and equitable plan for replacing non-productive Clinical Research Sites.

International Sites

6. Can non-U.S. based research organizations be identified as a Clinical Research Site in the application of a U.S. based CTU?

Yes. There are no restrictions as to how non-U.S. research organization can apply or how they can be identified within other applications. International organizations can be:

(1.) A Clinical Trials Unit, with one or more U.S. or international based Clinical Research Sites.
(2.) A Clinical Research Site affiliated with a U.S. based Clinical Trial Unit(s).
(3.) A Clinical Research Site affiliated with an internationally based Clinical Trial Unit(s).

7. How can researchers/institutions located in different countries that have worked successfully with NIH in the past be identified?

A database of all publicly available grants is available at: http://crisp.cit.nih.gov/ . It is also recommended that applicants inquire at their own institution, other institutions in their country, and with their Ministry of Health to identify local researchers that have successfully participated in NIH-sponsored research.

8. In some countries, discrepancies may exist between U.S. and local financial management and bookkeeping standards. What can applicants do to ensure that they meet the appropriate

criteria?

The NIH expects our grantees to follow existing U.S. policies and regulations concerning management and accounting. The NIH Grants Policy Statement (http://grants1.nih.gov/grants/policy/nihgps_2003/index.htm) is an excellent place to start looking at what policies and regulation you will need to follow.

It may be helpful for applicants with concerns in this area to engage in a Mentoring Partnership and utilize the relationship to learn how to meet the financial management and bookkeeping requirements of this particular RFA.

9. The perceptions of Good Clinical Practices (GCPs) may vary from country to country. Is there any guidance to help newer CTUs determine if their practices meet NIH standards?

NIAID relies upon the standards developed by the International Conference on Harmonization Guidance for Industry E6 Good Clinical Practice: Consolidated Guidance to determine its expectations for all Clinical Research Sites participating in NIAID-sponsored clinical trial research. As interpretations of these standards may vary, DAIDS may provide training and work with grantees, including Networks and CTUs, to ensure that they fully understand DAIDS expectations.

In cases where an institution is governed by country-specific regulations, the applicant must follow whichever guidelines are most stringent.

10. Can international Clinical Research Sites receive funding for renovations under this RFA?

The answer is no. This RFA does not allow for the support of physical renovations. The Clinical Research Sites proposed in applications are expected to have an appropriate infrastructure and be capable of initiating participant enrollment within six months of award.

11. Does the RFA discourage a U.S.-based CTU from having foreign Clinical Research Site components?

No, the RFA does not discourage a U.S.-based CTU from including foreign Clinical Research Sites. However, the RFA does encourage capable foreign institutions to submit applications for Clinical Trials Units. The Mentoring Partnership option is designed to facilitate the transition of experienced clinical research groups (both within and outside of the United States) from functioning as a site or sites in a U.S. based-CTU to an independent CTU.

Budget

12. Do applicants with budgets greater than $500,000 US dollars per year need to submit a letter requesting prior approval before submitting their application?

No. This is no longer required for solicited applications.

13. Should the costs of new trial participants enrolled (after the new award period) into ongoing protocols be included in the core budget using the template protocols on the web site or the actual cost of the protocols?

Core budgets should be based on the template protocols found on the DAIDS Clinical Trials Networks FY 06 website. Thus, the costs associated with trial participants enrolled after the new award period into protocols that began prior to the new award, which are included in the core budget, should be based on the template protocols. The protocol templates are located at http://www.niaid.nih.gov/daids/rfa/network06/units_protocol_schema.htm. These templates are based on actual DAIDS-funded studies and allow for consistency and flexibility in constructing the core budget.

NOTE: It has come to the attention of DAIDS that there is confusion about transition costs. Transition costs are described in the RFA as follows: "Transition Costs (Ongoing Costs at the Time of Award). For each applicable Clinical Research Site, ongoing costs should identify the financial resources required to continue protocol-required follow-up of participants enrolled through an existing DAIDS-sponsored Clinical Trials Network for Year 1 only." In Table 1B, Worksheet for Transition Costs, the planned enrollment field was intended for sites to identify the number of participants they intended to enroll into the study during the time period between submission of an application and receipt of a new award. It was not intended to identify participants that applicants planned to enter during year 1 under a new award and in a new/restructured DAIDS-sponsored Clinical Trials Network.

It is unfortunate that the extent of this confusion has only recently come to the attention of DAIDS. We wish to reassure applicants that this different interpretation will not have a significant impact on the process. We appreciate the difficulties in forecasting a year ahead, realize it is not possible to be exact, and recognize that unanticipated events will occur. DAIDS has emphasized that these transition budgets are important for planning purposes. CTU/Clinical Research Sites that include all potential participants on their transition budgets should be mindful that the core budget will be used to cover the costs of new enrollments into ongoing studies as well as new enrollments into new studies. Budget adjustments will, no doubt, need to be made based on the status of the transition studies and actual enrollments closer to the time the new awards are made and, of course, the funds available. These revised budgets should be able to accommodate modifications in projected enrollment and/or cost differentials between the template protocol and an actual transition study.

14. Should costs for trial participants included in the transition budget be based on the actual cost of the protocol or the template protocols?

Transition budgets should include the costs of ongoing trial participants and should be based on the actual cost of the protocol.

15. How should applicants budget for participant costs, such as adverse events that might lead to hospitalization?

Using past experience as a guide, applicants should estimate the types and number of

expected events based on the kinds of protocol(s) expected in the high priority research area(s) or network affiliation(s) in which the CTU plans to participate. These estimates should be used to calculate the financial requirements for repeat testing, management of the adverse events, following participants until the events resolves, etc. In some clinical research settings, this might include calculating the costs of treatment, including hospitalization.

16. If equipment is included in the budget but is no longer needed at the time of award, can funds allocated for this equipment be transferred and used to cover a different piece of equipment?

In general, NIH tries to allow for flexibility in these circumstances. However, in some cases, certain components of award are "restricted" and these restrictions will be listed under "specific grant-related terms and conditions." These terms delineate the specific types of changes that will require the prior approval of NIAID.

17. Where should administrative costs related to CABs be included in the budget?

The location of CAB-specific costs in the budget will depend on the purpose of the administrative cost. Many costs will probably fall under consultant costs (e.g., consultant fees and travel) but some costs may also fall under other categories, such as supplies.

18. Do transition costs apply to studies conducted as part of a CIPRA (Comprehensive International Program on AIDS) award?

No, CIPRA grantees are not directly affected by this competition. If a CIPRA grantee were to receive an additional award under this RFA, the applicant would need to work with DAIDS to eliminate any overlap that exists.

Research

19. How is the term "children" defined for purposes of the RFA?

The term "children" refers to anyone less than 21 years of age.

20. Is it permissible for participant populations to include undocumented aliens in research supported under this RFA?

There is no provision that excludes undocumented aliens from participating in research conducted under this RFA. Ultimately, the ability to include these populations in the clinical research will depend on the policies of the country and institution where the Clinical Research Site is located.

21. Can a CTU participate in research under this RFA as well as in projects funded by other U.S. agencies? Is NIAID approval required to do so?

Awardees under this RFA are eligible to work on projects funded by other U.S. agencies and do not require NIAID's permission to do so. Applicants currently participating in such projects should indicate these activities when describing their experience in the application. Applicants cannot propose any budgetary overlap in their application. Successful applicants will need to indicate if any scientific overlap exists at the time of award and must work with DAIDS to negotiate how to eliminate this overlap.

Mentoring Partnerships

22. With respect to a proposed Mentoring Partnership, what will happen to the mentee institution if the mentor institution is not funded?

If the mentee institution is successful under this RFA but the mentor is not, DAIDS will work with the mentee to identify suitable mentorship during the award period.

Review

23. Is there a mechanism to request that a particular individual in conflict is excluded from the review of a specific application?

NIAID has taken great care to establish mechanisms to avoid real or potential conflicts of interest during the review of applications. However, in exceptional circumstances applicants may contact the scientific review staff at NIAID if they are concerned that a specific potential conflict may not be identified. Please contact Dr. Greg Jarosik, (gjarosik@niaid.nih.gov) or Dr. Priti Mehrotra (pmehrotra@niaid.nih.gov) in the Scientific Review Program with specific concerns.

24. Will CTU applications be evaluated against applications received from institutions in the same country or geographic area?

CTU applications will be evaluated independently according to the review criteria delineated in the RFA. Applications will not be evaluated "against" each other.

25. Will a CTU have the opportunity to respond to the summary statement?

No, there is no opportunity for an applicant to respond to the summary statement.

26. Has DAIDS pre-established the number of sites or CTUs that will be awarded by geographic region?

Quotas have not been established for CTUs by research area or by geographic location. DAIDS plans to fund the number and type of CTUs and Clinical Research Sites that are appropriate to support the research proposed by the successful Network Leadership applicants.

27. Should applicants assume that reviewers will have knowledge of DAIDS-approved pharmacies (i.e. facilities with pharmacy plans approved by DAIDS)? If a proposed CTU contains a pharmacy with a pharmacy plan previously approved by DAIDS, should applicants include this information in the application?

Applicants should not assume that reviewers are aware that the pharmacy described in the application has a Pharmacy plan approved at DAIDS. Applicants may reference this prior approval, but should also provide a complete description of the pharmacy staff and facilities relevant to the proposed research areas.

Application Assembly

28. Please provide more details on how to list SOPs in the application. Is it necessary to include an exhaustive list of SOPs, or would a sample be acceptable?

Applicants should make an effort to convey that the Clinical Research Site(s) and the CTU conduct clinical research in accordance with Good Clinical Practices, including the existence of and adherence to standard operating procedures. This may be accomplished, for example, by discussing general procedures for establishing SOPS, listing SOPs used at their CTU, etc. Applicants may elect to use the Appendix to include a list of SOPs or to provide a synopsis of one or two SOPs as examples.

29. Is an eRA Commons user ID required for inclusion in CTU applications?

Applicants with an eRA Commons user ID (institutions that have previously participated in NIH-funded research) are requested to include this information with their application. However, the inclusion of a user ID in not a requirement of the application.

30. The application aims to capture a lot of information within 10 pages. Is it allowable for applicants to decrease the font size to provide more information?

No. Applications must follow the formatting guidelines set forth in the PHS 398 instructions. Applications that do not conform to these specifications will be returned without review.

31. Is a letter of commitment from a Network Leadership group a required component of a CTU application?

No, a letter of commitment is not a required element. However, if a commitment has not been obtained from a Network Leadership group, applicants must state which priority area(s) they plan to address.

32. Does the page limit for the appendix section include the CTU and the Clinical Research Sites?

The 30 page limit for the appendix is for the whole application, including the CTU and Clinical Research Sites.

33. In cases in which one institution will submit two CTU applications, where should language describing the rationale/necessity for the two CTUs be described?

Applicant institutions are discouraged from submitting more than one CTU application. Should this occur, however, applicants must describe the geographic, organizational or other barriers to effective sharing of resources; ensure collaboration; and minimize duplication of efforts and redundant costs. This information should be included in the letter of intent from each applicant and also included in the research plan of each application.

Community Advisory Boards

34. In the event that Clinical Research Sites within a given CTU are geographically disparate, should each Clinical Research Site have its own CAB? Similarly, if a CTU is located in one country and an affiliated Clinical Research Site is in another, should each entity have its own CAB?

The number of CABs within a given CTU is a decision best made by the applicant. This decision should take into account the role of the CAB in representing the local community participating in the clinical research and the geographic and cultural diversity of the Clinical Research Sites.

Federal Wide Assurances

35. Can two Clinical Research Sites share an FWA?

Each institution where a clinical site is located is required to have a Federal Wide Assurance (FWA). Therefore, two Clinical Research Sites affiliated with the same institution can share one FWA. Further information on FWA policies can be found at the Office of Human Research Protection web site: www.hhs.gov/ohrp/assurances/assurances_index.html .

35. Please explain the relationship between an FWA and the IRB. Does each Clinical Research Site need to have its own IRB?

Each institution where a clinical site is located is required to have an FWA. It is also required to designate an IRB, whose role is to approve and periodically review the research being conducted to ensure the adequate protection of human subjects. This IRB must be named in the FWA of the institution where the research will be performed. Clinical Research Sites located at the same institution may function under the same FWA. They may or may not have the same IRB. Please see the Office of Human Research Protections (www.hhs.gov/ohrp/assurances/assurances_index.html) for more information.

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